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Paricalcitol and calcitriol therapeutic effects, prospective comparison of adult hemodialysis patients

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ABSTRACT

This study aimed to compare the efficacy of a selective activator of the Vitamin D Receptor (VDR) paricalcitol with calcitriol, for the repression in terms of intact Parathyroid Hormone (iPTH) secretion. A comparative study was undertaken in order to determine whether paricalcitol provides a therapeutic advantage to calcitriol. The groups has formed adult hemodialysis individuals treated with dialysis solution three times (4 hours, each seans) per week for 8 months with 1.25 mmol/L calcium (Ca) bicarbonate dialysate. Patients with iPTH levels over 400 pg/ml were treated with paricalcitol. In addition, their iPTH levels over 295 pg/ml were treated with calcitriol. The treatment was cut of both paricalcitol and calcitriol over CaxP > 65 and iPTH <295 pg/mL. The cure was regulated according to levels iPTH in patients both paricalcitol and calcitirol. The application was a rule as particular posthemodialysis. The patients were administered intravenosus paricalcitol 5-10 mcq and calcitriol 1-2 mcq as bolus. Diet restriction was referenced to reduce P levels. All the patients have been screened with parathyroid gland ultrasound and parathyroid scintigraphy. Compared to initial value we achieved 39.3% reduction in the group 2 iPTH concentration (569 pg/mL to 345 pg/mL). On the other hand iPTH concentration has been identified as 337 pg/mL initially while the mean value was 357 pg/mL at the study end of in the group1. In other words the mean average iPTH values is not reduced in group1. These results between Group 1 and Group 2 was statistically significant. As a result paricalcitol much more rapidly and meaningful to reduced according to calcitriol of iPTH levels in serum. On the other hand we have not found difference between two groups with minimal advers effect.

Key words: End-Stage Renal Disease (ESRD), Calcitriol, Corrected CaxP, Paricalcitol.

INTRODUCTION

Vitamin D increases the intestinal absorption of calcium channels, in addition to this property both bone deposition, as well as a hormone that makes bone resorption. Despite all the characteristics of an active substance of vitamin D by itself is not capable of these functions. First the consecutive reactions in the liver and kidneys is the product of active vitamin D 1,25 - dihydroxi-cholecalciferol need to turn into [1]. Cholecalciferol is composed significantly in the skin 7 - hydroxi-cholecalciferol with the effects of the sun's ultraviolet rays. Nutrients is taken with vitamin D almost identical to cholecalciferol. Cholecalciferol 25 - hydroxi-cholecalciferol first phase transformation occurs in the liver. This process of realization self-checking feature. This feedback is important to control the process two points, the first of which the plasma 25 – hydroxi-cholecalciferol very sensitive to the concentration of the layouts. Second, vitamin D3, 25 - in the body after conversion to hydroxi-colecalsiferole controlled in this way can stay a few weeks do not undergo the transformation of the liver and can be stored for months. The most active form of vitamin D in kidney proximal tubules dihydroxi-cholecalciferol 1.25, transformation 25 – hydroxi-cholecalciferol absence of kidney or renal failure in stage V, leads to the destruction of large amounts of vitamin D effect. Parathyroid hormone in the kidneys of the necessity of this transformation is a fact that should not be forgotten, that the hormonal conversion would not be without PTH. Without vitamin D; parathyroid hormone activity on the other hand, does not namely calcium and phosphate metabolism, bone and tooth building, vitamin D, parathyroid hormone (PTH), calcitonin regulation correlated with each other [2]. With vitamin D analogues paricalcitol, the new limits are being developed and a highly effective preparat. Paricalcitol first in-vitro - studies was of animal experiments [3]. Both the drugs dose adjustments were based on laboratory results for iPTH, calcium, and CaxP. The firstly end point cut off more less than 295 pg/ml (iPTH) the treatment. Secondly end point cut off the treatment the occasion of raise high CaxP >65. In our study we aim to feature a prospective study in ESRD adult hemodialysis patients with an increasing bone disease the widespread use of calcitriol paricalcitol and find out whether one of them has advantages to the other one.

EXPERIMENTAL SECTION

Our study is based on the patient volunteer double-arm, prospective with an experimental content, data evaluation of parallel design, the active drug controlled. The study was took between December 2008 - July 2009 for 8 months. Working has been done in the special on hemodialysis treatment center (“Ozel Konya Huzur Diyaliz Merkezi” Konya/TURKEY). Total 35 patients were included, they were 69-75 years of age. The study was approved by local ethical committee. In the study of two vitamin D analogue is used in two separate group of patients. Group 1 (calcitriol) consists of people accept this treatment on their iPTH levels 295 pg/ml and above. Group 2 (paricalcitol) consists of people accept this treatment on a voluntary basis their iPTH levels 400pg/ml and above. The application was a rule as particular posthemodialysis. The cure was regulated according to levels iPTH in patients both paricalcitol and calcitirol.

Treatment groups were applied as follows;
Group1: iPTH > = 295 pg/mL and < 700 pg/mL as calcitiol 3x1mcq (weekly total 3 mcq), iPTH > =700 pg/mL and < 1000 pg/mL as calcitriol 2x2mcq (weekly total 4 mcq), iPTH > = 1000 pg/mL as calcitriol 3x2mcq (weekly total 6 mcq).

Group2: iPTH > = 400 pg/mL and < 700 pg/mL as paricalcitol 3x5mcq (weekly total 15 mcq), iPTH > = 700 pg/mL and < 1000 pg/mL as paricalcitol 2x10mcq (weekly total 20 mcq), iPTH > = 1000 pg/mL as paricalcitol 3x10mcq (weekly total 30 mcq).

Although single-center study patients used drugs in blood serum iPTH during the eight months were noted, “Corrected Ca”, P, “Corrected CaxP”, followed by the effects on the data registration forms. All the patients according to levels of serum albumin, serum Ca levels were calculated using the following formula: corrected Ca (mg/dl) = measured total Ca + 0.8 x (4 – albumin in the serum) [2]. Patients have been adopted with vitamin D analogue as the criteria for discontinuation of treatment “Corrected CaxP” > 65 and iPTH values < 295pg/mL. The blood samples were taken as predialysis all in the patients. The samples of centrifugal device separated after coagulation process. Their sent to the relevant laboratory in accordance with the cold chain. In the laboratory were used in which the VITROS 5.1 VITROS FS Architect 2000 SR 950 devices and Abott and Beckman Coulter Access 2 devices. All of the patients three seance per week were at least four hours of treatment with bicarbonate hemodialysis and demonstrated sensitivity this condition. Because studies are shows that affects irregular seance full blood biochemistry values in dialysis patients. All our patients were functional the objectives of the treatment, the choice of phosphate binder given attention to the values and special restrictive phosphorus dietary.

Statistically: this study were used ratio and proportion tests.
Ethic: this study ethic committee report was taken as local.

Criteria for inclusion in working groups

1. Adult hemodialysis patients to accept to treatment three seance in the week and each seance minimal four hours and bicarbonate therapy.
2. Phosphorus-rich foods diet restriction, oral intake of calcium and albumin-supported diet, dialysate calcium 1.25 mmol/L in the selection of drug use and antifosfat Ca according to the level necessary to accept the use of Ca-free preparate.
3. Calcitriol drug therapy to begin "the serum iPTH> = 295 pg/mL and <400 pg/ml, serum “Corrected CaxP” <65 . For cut of treatment the corrected CaxP> 65 and iPTH < 295 pg/ml.
4.Paricalcitol drug therapy to begin iPTH>= 400 pg/ml and over in the serum, the level of serum corrected CaxP <65. The treatment is for cut of the corrected CaxP> 65 and iPTH <295 pg / ml.

Table 1: criteria for working groups; Group1 and Group2

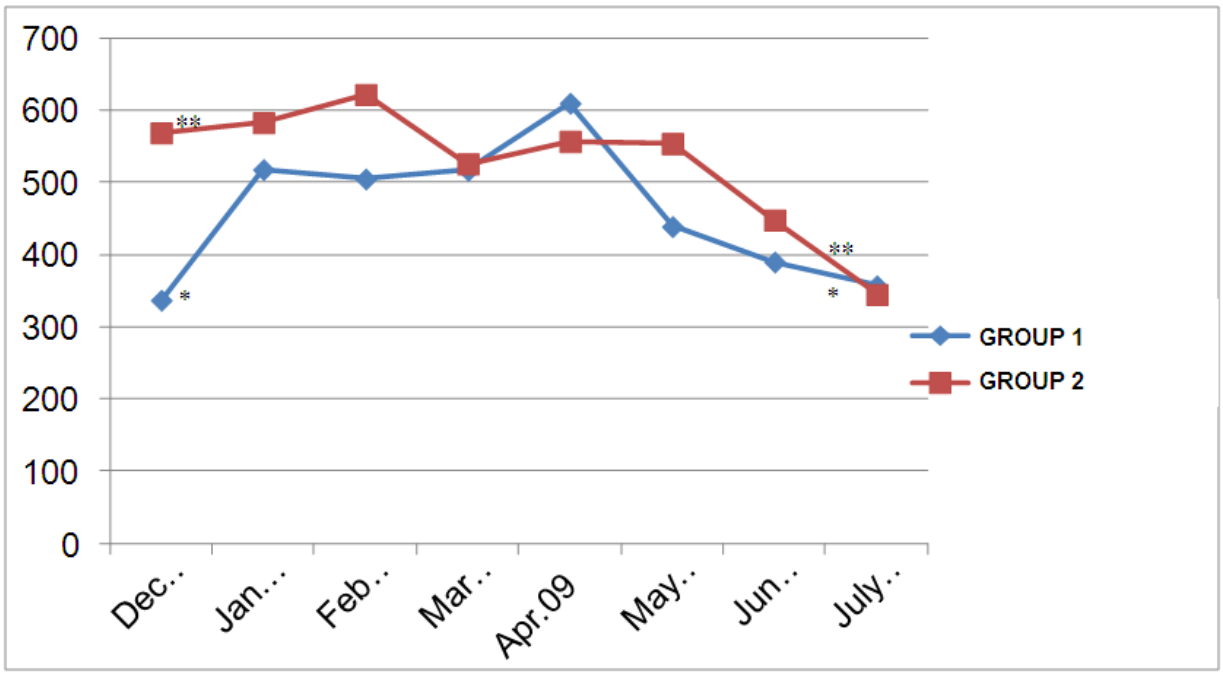
Groups	iPTH range values	I.V.Cure
Group1	iPTH >= 295 pg/mL and < 700 pg/mL	3x1mcq
	iPTH >=700 pg/mL and < 1000 pg/mL	2x2mcq
	iPTH >= 1000 pg/mL	3x2mcq
Group2	iPTH >= 400 pg/mL and < 700 pg/mL	3x5mcq
	iPTH >= 700 pg/mL and < 1000pg/mL	2x10mcq
	iPTH >= 1000 pg/mL	3x10mcq

Group 1: "calcitriol" control group was formed according to the criteria described in the inclusion. Group 2: "paricalcitol" group was formed both voluntary basis and the criteria described in the inclusion. Intravenous treatment protocols was applied during eight months in table 1 generated by groups.

RESULTS

In this study the target iPTH values, within the time frame of eight months, some groups have been reached earlier in patients. However, treatment protocols and the treatment is stopped again, started to be increased in these patients had to be re-iPTH values. The patients of whom irregular treatment uses calcitriol and paricalcitol have not been identified difference between in the group 1 and group 2. Some patients achieved the target iPTH value viewed used the average values of iPTH, the mean value of iPTH 432 pg/mL users of paricalcitol, calcitriol users this value is determined as 402 pg/mL after a month start treatment. Our study was to achieve treatment goal iPTH values as 39.3%, in the number of the patients 32 weeks in late Group2. On the other hand this values were found some patients of whom in regular treatment for paricalcitol 509 pg/ml and for calcitriol 614 pg/ml. Furthermore have been reached the target iPTH value of the average values of patients after the 8 months. The study evaluated 70 patients overall iPTH levels were significantly reduced over a long-term (32 week). This study are found with minimal hyperphosphatemia and hyper calcemia in this adult ESRD patients (two patients in all the groups).

Figure1: Group1 and Group2 mean iPTH during 8 month of drug administration (pg/mL)



The study was began December 2008 and ended in July 2009. Figure 1 shows us according to the paricalcitol (group2) calcitriol (group1) much more rapidly and meaningful to reduced iPTH values in serum (**p<0.05). Thus, paricalcitol was showed 39.3% acording to calcitriol in a more rapid decrease in iPTH concentrations. Group 1 patients has been determined statistically not significant (*p >0.05).

Table 2: all the patients average monthly values of iPTH all the groups

	Dec.08	Jan.09	Feb.09	Marc.09	Apr.09	May.09	June.09	July.09
Group1	337pg/mL	518pg/mL	505pg/mL	517pg/mL	610pg/mL	439pg/mL	390pg/mL	357pg/mL
Group2	569pg/mL	583pg/mL	622pg/mL	526pg/mL	557pg/mL	554pg/mL	448pg/mL	345pg/mL

There are statistically significant difference between group 1 and group2 ($P < 0.05$). Group 2 patients has been determined reduction proportion in 39.3%, such that of the study iPTH value at the beginning 569 pq/mL and the end of 345 pg/mL (statistically significant, $p < 0.05$). On the other hand Group 1 patients has been determined increase proportion in 5.9%, such that of the study iPTH value at the beginning 337 pq/mL and the end of 357 pg/mL (statistically not significant, $p > 0.05$).

DISCUSSION

Previous clinical studies of paricalcitol had worked "paricalcitol with calcitriol-resistant secondary hyperparatroidism in dialysis patients" [6]. This similarity seems to be particularly significant in terms of methods and findings. Furthermore a special diet had been taken as the limitted out of phosphorus in both studies patients. In our study was cut-of paricalcitol therapy 2 cases, because of CaxP level > 65 so occurs hyperphosphatemia. The other study paricalcitol was preferred over 600 q/mL iPTH value but in our study were chosen as the 400 pg/mL [9]. In our study CaxP <65 was accepted as a criterion to start treatment (NF-K/DOQI according to current), the another was considered for the value CaxP <75 in the another similar study [10]. The another smilar working included the average age of 54 ± 15 (22-90) in adult patients. This working is named “Paricalcitol versus calcitriol in the treatment of secondary hyperparatroidism" and have been 32 weeks to study for the implementation of adult hemodialysis patients [12]. In this study, paricalcitol 's efficacy to reduce iPTH were found as %50. In our study we achieved 39.3% treatment goal for iPTH values in 32 weeks in late Group2. While the other study Calcitriol 's effectivity have been detected as 25% [12]. A study smilar to our study, made in Turkey [14]. Their study was prospective with adult hemodialysis patients. Their paricalcitol target value was determined as %66. Our study found the target value as 39.3% for iPTH reduction. Their target value to cut-off paricalcitol was 300 pg/mL but in our study the cut-off was <295.

CONCLUSION

Our study showed that paricalcitol reduced much more rapidly serum levels of iPTH than calcitriol. Further more reductions was found significiant. There were several differences between the two groups (group1 and group 2), which suggest that paricalcitol might be safer. Patients showed consistent progression toward target iPTH levels, but early cut off intreatment might rise iPTH levels. Although they suggest a therapeutic advantage to the use of paricalcitol. On the other hand no difference was found between the two groups in the "CaxP" values at least during treatment.

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